Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the editor

Anosmia during acute COVID-19 and psychiatric outcomes 4 months later: Results from the prospective COMEBAC cohort

>600 million individuals have been infected with SARS-CoV-2 (COVID-19). Olfactory deficits, chiefly anosmia, are frequent during acute COVID-19 infection. Anxiety, depression, and post-traumatic stress are highly prevalent in the months following acute COVID-19 infection, particularly after hospitalization [6]. Indeed, anxiety disorders and major depressive disorders are diagnosed in 11%–19.5% and 13%–15.9% of patients following acute COVID-19 infection, respectively [2,3,5,7,8].

Olfactory deficits have been associated with mental disorders [1]. This association has been further elucidated by the COVID-19 pandemic. Indeed, two pioneer studies [4,9] reported associations between anosmia and psychiatric symptoms during acute COVID infection. However, to our knowledge, no prospective study assessing anosmia during acute COVID-19 infection and the development of psychiatric symptoms and disorders several months later has been performed.

This study aims to assess the association between anosmia during acute COVID-19 infection and the development of psychiatric symptoms and disorders four months after hospitalization.

Methods are detailed in supplementary (S1). One hundred seventy-seven patients were assessed four months after hospitalization for acute COVID-19 infection. Patient characteristics are presented in Table 1. Sixty-two (35%) patients had anosmia during acute COVID-19 and 115 (65%) did not. Compared to patients without anosmia during acute COVID-19 infection, those with anosmia were more often female (Table 1). Seventeen patients had a history of psychiatric disorders (Table 1). Among them, 16 were psychiatrically stable before acute COVID-19 infection.

Compared to patients without anosmia during acute COVID-19 infection, those with anosmia had significantly more symptoms of depression (BDI), anxiety (HAD-A), post-traumatic stress (PCL-5), and insomnia (ISI), as well as more anxiety disorders 4 months after hospitalization (Table 1 and Fig. S2). After adjusting for sex, age, and ICU (intensive care unit) stay, anosmia during acute COVID-19 infection was associated only with symptoms of depression (estimate = 1.82; 95%CI [0.76–3.15]; $p = 0.044$) and post-traumatic stress (estimate = 5.1; 95% CI[1.6–8.0]; $p = 0.03$) 4 months after hospitalization. After adjusting for the duration of COVID-19 hospitalization, this association was significant for all psychiatric symptoms as well as for anxiety disorders (Table S4).

In the 160 patients without a history of psychiatric disorders, those with anosmia during acute COVID-19 infection had significantly more symptoms of post-traumatic stress and insomnia 4 months after hospitalization (Table S3). The association with symptoms of post-traumatic stress remained significant after adjusting for the duration of COVID-19 hospitalization ($p < 0.05$), but not after adjusting for sex, age, and ICU stay.

In the 17 patients with a history of psychiatric disorders, those with anosmia during acute COVID-19 infection had significantly more symptoms of depression, anxiety, and post-traumatic stress and current psychiatric disorder 4 months after hospitalization (Table S3 and Fig. S2), even after adjusting for sex, age, ICU stay, and COVID-19 hospitalization duration (Table S5).

This is the first prospective observational study examining the association of anosmia during COVID-19 infection with subsequent psychiatric symptoms and disorders. In patients hospitalized for acute COVID-19 infection during the first wave of the pandemic, anosmia during acute COVID-19 infection was associated with more symptoms of depression and post-traumatic stress 4 months after hospitalization. Among patients with a history of psychiatric disorders, anosmia during acute COVID-19 infection was associated with symptoms of depression and post-traumatic stress and psychiatric disorders after hospitalization.

The frequency of acute anosmia (35%) is in line with previous results among patients hospitalized for acute COVID-19 infection. We observed more anosmia during acute COVID-19 infection in females compared to males, which also agrees with previous results [4].

Two previous studies have reported an association between anosmia during acute COVID-19 infection and psychiatric symptoms [4,9]. Our results go beyond these two pioneer studies by showing that anosmia during acute COVID-19 infection predicts psychiatric outcomes 4 months after infection. Our findings suggest that acute anosmia may reflect locoregional inflammation in the limbic system and/or that sensitivity to olfaction could be a risk marker for psychiatric outcomes.

Nevertheless, this study has several limitations. First, its small sample size. Second, anosmia was assessed naturalistically and not objectively. Nevertheless, there are feasibility issues for objective olfactory testing during the acute phase of severe COVID-19 infection, and anosmia is easily detected in current practice. Third, only those patients treated in the ICU or those with persistent symptoms 4 months after hospitalization were included and were thus not representative of all hospitalized patients with COVID-19. Lastly, psychiatric disorder history was extracted from medical records. Thus, it is possible that some events were underestimated, even if assessment was performed by trained psychiatrists, increasing the certainty of identified cases.

In conclusion, anosmia during acute COVID-19 infection is associated with higher rates of psychiatric outcomes 4 months after hospitalization, particularly in patients with a history of psychiatric disorders. Patients with a history of psychiatric disorders and anosmia during acute COVID-19 infection may benefit from psychiatric screening.

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Table 1
Baseline characteristics and psychiatric outcomes of patients with and without anosmia during acute COVID-19 infection.

	Total sample (n = 177)	Anosmia during acute COVID-19 infection (n = 62)	No anosmia during acute COVID-19 infection (n = 115)	p
Age m (sd)	56.9 (13.2)	54.9 (13.2)	58.9 (13.2)	0,09
Female n (%)	68 (38.4)	34 (54.8)	34 (29.6)	**<0.01**
Active smoking n (%)	15/169 (8.9)	2 (3.3)	12 (10.8)	0.25
Psychiatric disorder history n (%)	17 (9.6)	6 (9.7)	11 (9.6)	0.97
Past Major depressive disorder n (%)	14 (7.9)	6 (9.7)	8 (7)	0.60 0.66 0.73
Past Anxiety disorder n (%)	1 (0.6)	0 (0)	1 (0.9)	
Others n (%)	2 (1.1)	0 (0)	2 (1.8)	
Past psychotropic drugs n (%)	23 (13)	6 (10.0)	17 (15.3)	0.32
Antidepressants n (%)	11 (6.2)	4 (6.6)	7 (6.3)	0.82
Other psychotropic drugs n (%)	12 (6.8)	2 (3.3)	10 (9)	0.37
Hospitalization in ICU n (%)	97 (54.9)	28 (46.6)	69 (62.2)	0.10
Duration of COVID-19 hospitalization (days) m (sd)	22 (16.2)	20.3 (15.9)	24.7 (20.9)	0.54
BDI m (sd)	4.8 (5.0)	6.2 (6.2)	3.9 (4.0)	**<0.05**
HAD-A m (sd)	5.7 (4.0)	6.8 (4.5)	5.1 (3.6)	**<0.05**
PCL-5 m (sd)	13.1 (13.3)	17.4 (16.1)	10.7 (10.8)	**<0.01**
ISI m (sd)	15.2 (13.7)	18.7 (14.1)	13.2 (13.1)	**<0.05**
Current psychiatric disorder n (%)	36 (20.3)	17 (27.4)	19 (16.5)	0.21
Major depressive disorder n (%)	24 (13.6)	11 (17.7)	13 (11.3)	0.23
Anxiety disorder n (%)	20 (11.3)	12 (19.3)	8 (7.0)	**<0.05**
PTSD n (%)	7 (4.0)	4 (6.5)	3 (2.6)	0.21

Legends: BDI: Beck Depression Inventory; HAD-A: Hospital Anxiety and Depression scale Anxiety; ICU: intensive care unit; ISI: Insomnia severity Index; m: mean; PCL-5: Posttraumatic Stress Disorder Checklist for DSM-5; PTSD: Post-traumatic stress disorder; sd: standard deviation.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.genhosppsych.2023.06.003.

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